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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/506,942	BALLOUL ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,36,38,40,44,46,48,49,53-56,62,64,65,69,71-75,79 and 80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,36,38,40,44,46,48,49,53-56,62,64,65,69,71-75,79 and 80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/043933.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32, 36, 38, 53 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowy et al. (US 5,618,536), Hagensee et al. (Journal of Virology. 1993; 67 (1): 315-322), Borysiewicz et al. (Lancet. June, 1996; 347: 1523-1527), Galloway (Infectious Agents and Disease. 1994; 3: 187-193), and Meyer et al. (Journal of General Virology. 1991; 72: 1031-1038), as further evidenced by Boursnell et al. (US 5,719,054) for reasons of record.

Applicant states that the VLPs of Lowy et al. mimic the structure and morphology of the virus. However, this statement is contradicted by the next statement, which points out that E7, is also exposed on the surface of the VLPs. Wild-type papillomavirus virions do not express or expose early polypeptides, such as E7, on the surface.

Applicant also argues that Lowy et al. fail to demonstrate any therapeutic efficacy against pre-existing HPV tumors with the VLPs disclosed.

Applicant's arguments have been fully considered, but are found unpersuasive. The instant claims do not require therapeutic efficacy with L1 and L2 polypeptides. The instant claims require a pharmaceutical composition consisting of an MVA vector that independently expresses E6, E7, L1 and L2. The instant composition is used in a method of treatment or prevention of papillomavirus infection. Since it is clearly evident from the combination

teachings in the prior art cited that L1 and L2 papillomavirus polypeptides are prophylactic and that E6 and E7 papillomavirus polypeptides are therapeutic (see pages 5-6 in the advisory action mailed 9/1/4 for a summary of citations), it is prima facie obvious that a composition comprising these therapeutic and prophylactic elements would be therapeutic and prophylactic (emphasis added). Contrary to applicant's assertions, Lowy et al. do teach that L1 and L2 polypeptides are protective against papillomavirus infection, see column 2, lines 60 to column 3, line 16, column 7, lines 35-61 and example 9 in column 14. As admitted by applicant on page 12, Hagensee et al. also teach prophylactic efficacy using L1 and L2 genes. One of ordinary skill in the art at the time the invention was made would have been motivated to combine the prophylactic papillomavirus polypeptides of Lowy et al. and Galloway with the therapeutic papillomavirus polypeptides of Galloway, Lowy et al., and Borysiewicz et al. to treat or prevent papillomavirus infection in a single composition. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because L1 and L2 possess prophylactic properties (discussed by Lowy et al. and Galloway) and E6 and E7 possess ameliorative properties (discussed by Borysiewicz et al. and Galloway).

Regarding the teachings Boursnell et al., applicant concludes that the reference as a whole teaches fused expression of papillomavirus proteins merely because only one example of un-fused polypeptides is provided. However, the explicit teaching of un-fused expression of papillomavirus proteins, found in Figure 26c, column 3, lines 29-35 and column 8, lines 24-37, does not detract from the express disclosure of the un-fused embodiment.

Applicant also cites the paragraph of Boursnell et al., bridging columns 9 and 10, that discusses fusing E6 and E7 due to possible difficulties for achieving independent expression.

Applicant states that the skilled artisan would not have a reasonable expectation of success for expressing multiple genes from different promoters within a vaccinia virus vector.

Applicant's arguments have been fully considered, but are found unpersuasive. It appears that applicant is misinterpreting the discussion of Boursnell et al. In the same paragraph applicant points to, Boursnell et al. explain the reason for the possible difficulty, due to extraneous marker sequences, and also explain how the difficulty is obviated. Boursnell et al. teach that methods of insertion have been developed to allow elimination of the extraneous marker sequences, see column 10, lines 1-8. Further, the instant claims do not allow for any extraneous marker sequences. Therefore, the remote concern that multiple gene expression may be problematic in vaccinia vectors is eliminated by the new methods of insertion, discussed by Boursnell et al., and the fact that the instant vector does not include any extraneous selectable marker sequences. Boursnell et al. provide four examples of four HPV nonfused genes in Figure 26c (also see column 3, lines 29-35 and column 8, lines 24-37). Therefore, it is maintained that the ordinary artisan would have had a reasonable expectation of success for expressing multiple genes from different promoters in a vaccinia virus vector.

Applicant asserts that Galloway does not teach the use of un-fused L1 and L2 polypeptides.

In response, Galloway mentions "L1 or L2 fusion proteins" in the alternative in the second column on page 190. However, the reference does not specify what L1 or L2 are fused to. Since Galloway mentions the proteins in the alternative, they are obviously not fused to each other. Galloway also reviews vaccinia virus recombinants alternatively expressing early genes that retard the development of tumors, see the paragraph bridging pages 190-191.

Applicant summarizes the limitations of the invention and asserts that the required elements are not disclosed or suggested.

However, this assertion is clearly not the case. For applicant's convenience, recitation of the instant limitations and which references explicitly teach the limitations are presented below (emphasis added):

A composition consisting of:

A recombinant modified Ankara vector (MVA)

- Meyer et al. teach the vaccinia virus strain MVA, see pages abstract and pages 1032-1034.

with DNA sequences coding for (i) the early E6 and (ii) early E7 polypeptides of a papillomavirus and

- Galloway reviews the state of the art at the time the invention was made and teaches that the early papillomavirus polypeptides E6 and E7 are therapeutic in nature, see the abstract and pages 190-191.
- Lowy et al. suggest incorporating early papillomavirus polypeptides E6 and E7 into compositions to provide a therapeutic effect, see column 2, line 60 to column 3, line 16 and column 7, lines 35-61.
- Boursnell et al. claim a recombinant vaccinia virus vector expressing E6 and E7 early papillomavirus genes, see claims 1-3, 5, 8 and 12.
- Borysiewicz et al. teaches expression of early papillomavirus polypeptides E6 and E7 from a vaccinia virus vector to treat cervical cancer, see page 1524.

(iii) the late L1 and (iv) the late L2 polypeptide of the papillomavirus

- Galloway reviews the state of the art at the time the invention was made and teaches that the late papillomavirus polypeptides L1 and L2 are prophylactic in nature, see the abstract and pages 190-191.
- Lowy et al. teach a DNA molecule directing the expression of papillomavirus late polypeptides, L1 and L2, see claims 16, 17 and column 4, line 62 to column 5, line 2 to lines 6-9. Lowy et al. also teach that the papillomavirus late polypeptides are prophylactic, see column 2, lines 60 to column 3, line 16, column 7, lines 35-61 and example 9 in column 14.
- Hagensee et al. teach expressing papillomavirus late L1 and L2 proteins in a vaccinia virus, see pages 316-317.

wherein each of the DNA sequences under the control of independent expression elements

- Boursnell et al. clearly demonstrate the expression of four different papillomavirus gene sequences from different promoters in a vaccinia virus vector, see Figure 26c, column 3, lines 29-35 and column 8, lines 24-37.

the promoter necessary for the expression of the DNA sequences are: 7.5K and K1L genes

- Hagensee et al. teach expressing the late papillomavirus polypeptides, L1 and L2, in a vaccinia virus vector from a 7.5K promoter, see pages 316-317.
- Borysiewicz et al. teach expressing early papillomavirus polypeptides, E6 and E7, from a 7.5K promoter in a vaccinia virus vector, see page 1524.
- Meyer et al. teach that the insertion of the K1L genes in the MVA vaccinia strain leads to increased host range, see page 1037.

the DNA sequences are inserted into at least one excision region of MVA selected from: I, II, III, IV, V, VI and VII

- Meyer et al. teach six major deletion sites, I, II, III, IV, V and VI, that are not essential to virus replication in the wild-type Ankara strain and attenuates virus pathogenicity to MVA, see page 1032-1034.

a method of treating or preventing papillomavirus infection, dysplasia or cancer of the neck of the uterus by administering an effective amount of the composition and a pharmaceutically acceptable carrier

- Galloway reviews the state of the art at the time the invention was made and teaches that the late papillomavirus polypeptides L1 and L2 are prophylactic in nature, see the abstract and pages 190-191.
- Lowy et al. teach protection against papillomavirus infection with late polypeptides, L1 and L2, see column 2, line 47 to column 3, line 16, column 7, lines 35-61 and example 9 in column 14.
- Galloway reviews the state of the art at the time the invention was made and teaches that the early papillomavirus polypeptides E6 and E7 are therapeutic in nature, see the abstract and pages 190-191.
- Borysiewicz et al. teach expression of early papillomavirus polypeptides E6 and E7 from a vaccinia virus vector to treat cervical cancer, see page 1524.

Therefore, contrary to applicant's assertion, the combination of prior art references cited do teach every element of the claimed invention. Applicant has not pointed to an element in the instant claims that is not expressly taught by the combination of references.

Applicant also asserts that the combination of references does not provide a reasonable expectation of success for enabling independent expression of papillomavirus polypeptides from an MVA vector for efficacious presentation to the immune system. Applicant only cites the teachings of Lowy et al. to illustrate these assertions, although there are five other references with overlapping teachings cited in the instant rejection. More specifically, applicant states that the neutralizing antibodies induced by Lowy et al. are not indicative of success for the instant construct. Applicant also differentiates Lowy et al. from the present invention by pointing out that the E7 polypeptide of Lowy et al. is expressed on the surface of a VLP. Applicant asserts that the VLP of Lowy et al. may not correlate with a protective antitumor effect. Applicant concludes that the cited references teaching fusion of early polypeptides to L2 would not motivate the skilled artisan to make an un-fused papillomavirus polypeptides.

Applicant's assertions have been considered, but are found unpersuasive since the data presented combination of references indicates an antitumor activity (emphasis added). As discussed above, Galloway reviews the state of the art and concludes that papillomavirus polypeptides E6 and E7 are therapeutic and L1 and L2 have protective properties. Borysiewicz et al. teach expression of early papillomavirus polypeptides E6 and E7 from a vaccinia virus vector to treat pre-existing cervical cancer, see page 1524 and Hagensee et al. teach expressing papillomavirus late L1 and L2 proteins in a vaccinia virus, see pages 316-317. Although Hagensee et al. do not teach protective efficacy with L1 and L2, Lowy et al. do, see column 2, line 47 to column 3, line 16, column 7, lines 35-61 and example 9 in column 14. Although Borysiewicz et al., Hagensee et al. and Lowy et al. do not teach expressing each of the four papillomavirus polypeptides, E6, E7, L1 and L2 from individual expression control elements

from a vaccinia vector, Boursnell et al. clearly demonstrate the expression of four different papillomavirus gene sequences from different promoters in a vaccinia virus vector, see Figure 26c, column 3, lines 29-35 and column 8, lines 24-37. The vaccinia virus vector of Boursnell et al. is not MVA. However, Meyer et al. teach six major deletion sites, I, II, III, IV, V and VI, that are not essential to virus replication in the wild-type Ankara strain and attenuates virus pathogenicity to MVA, see page 1032-1034.

The combination of references clearly shows that expression of papillomavirus early polypeptides, E6 and E7, expressed from a vaccinia virus vector results in a therapeutic effect and that expression of papillomavirus late polypeptides, L1 and L2, expressed from a vaccinia vector, results in a prophylactic effect. Independent expression of four different papillomavirus polypeptides in a vaccinia virus vector is also expressly taught.

Therefore, it is maintained that one of ordinary skill in the art at the time the invention was made would have been motivated to express the HPV polypeptides of Lowy et al., Hagensee et al., Borysiewicz et al. and Galloway in the MVA vector of Meyer et al. under the control of different promoters, taught by Boursnell et al. to express the proteins from independent control elements in order to control transcription and subsequently, the amount of protein expressed in the cell. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of producing the construct claimed because Boursnell et al. teach individual expression of different HPV polypeptides in a vaccinia vector and MVA of Meyer et al. is a vaccinia vector.

Moreover, fusing E7 to the surface of a VLP is not instantly claimed. It is clear that no fusion is claimed, i.e. E7 to L2. The teachings of Lowy et al. are provided to demonstrate that

the late polypeptides, L1 and L2, induce a protective effect. Galloway arrives at the same conclusion in the review article presented. The teachings of Lowy et al. are also not cited for teaching therapeutic efficacy because the reference does not include those essential polypeptides, E6 and E7, into the composition. The inclusion of E6 and E7 in the composition of Lowy et al. to provide therapeutic efficacy is only suggested. Both Lowy et al. and Galloway separately teach protection against papillomavirus infection with L1 and L2, not treating a previously infected host with the two proteins. Neither Lowy et al. nor Galloway are cited for teaching expression of these prophylactic proteins in a vaccinia virus vector, i.e. MVA, because Hagensee et al. teach the expression of L1 and L2 from a vaccinia vector and Meyer et al. teach an MVA vector.

Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lowy et al. (US 5,618,536), Hagensee et al. (Journal of Virology. 1993; 67 (1): 315-322), Borysiewicz et al. (Lancet. June, 1996; 347: 1523-1527), Galloway (Infectious Agents and Disease. 1994; 3: 187-193), and Meyer et al. (Journal of General Virology. 1991; 72: 1031-1038), as further evidenced by Boursnell et al. (US 5,719,054), as applied to claims 32, 36, 38, 53 and 54 above, and further in view of Crook et al. (Cell. 1991; 67: 547-556) and Munger et al. (EMBO Journal. 1989; 8: 4099-4105) for reasons of record.

Applicant resubmits that in reference to the arguments presented for claim 32, none of the references provide disclosure or motivation for the skilled artisan to use an MVA vector independently expressing nonfused E6, E7, L1 and L2.

One of skill in the art at the time of the invention would have been motivated to combine E6 and E7 of Borysiewicz et al. into the vaccinia vector of Hagensee et al. expressing the L1 and

L2 proteins of Lowy et al. to treat and prevent papillomavirus infection in a host with the same administrative composition (emphasis added). One of skill in the art at the time of the invention would also have had a reasonable expectation of success for producing the claimed invention because L1 and L2 possess prophylactic properties (discussed by Lowy et al. and Galloway) and E6 and E7 possess ameliorative properties (discussed by Borysiewicz et al. and Galloway) (emphasis added).

One of ordinary skill in the art at the time the invention was made would have been motivated to express the HPV polypeptides of Lowy et al., Hagensee et al., Borysiewicz et al. and Galloway in to the MVA vaccinia vector of Meyer et al. under the control of different promoters, taught by Boursnell et al. to express the proteins from independent control elements in order to control transcription and subsequently, the amount of protein expressed in the cell. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of producing the construct claimed because Boursnell et al. teach individual expression of different HPV polypeptides in a vaccinia vector and MVA of Meyer et al. is a vaccinia vector.

Claims 44, 46, 48, 55, 56, 62 and 64 rejected under 35 U.S.C. 103(a) as being unpatentable over Lowy et al. (US 5,618,536), Hagensee et al. (Journal of Virology. 1993; 67 (1): 315-322), Borysiewicz et al. (Lancet. June, 1996; 347: 1523-1527), Galloway (Infectious Agents and Disease. 1994; 3: 187-193), and Meyer et al. (Journal of General Virology. 1991; 72: 1031-1038), as further evidenced by Boursnell et al. (US 5,719,054), as applied to claims 32, 36, 38, 53 and 54 above, and further in view of Bubenik et al. (International Journal of Oncology. 1996; 8: 477-481) for reasons of record.

Applicant submits that Bubenik et al. neither disclose or suggest all of the elements required by the instant claims.

However, the combination of references not only teach all of the limitations recited, but also provide a motivation and reasonable expectation of success for arriving at the claimed invention. If any single reference taught all of the limitations presented, the reference would have been considered under a different statute, i.e. 35 USC § 102.

Applicant further submits that the motivation presented in the Office action for expressing IL-2 in an MVA expression vector to avoid administering multiple injections of IL-2 is incorrect. However, applicant contradicts this assertion in the previous paragraph on page 17 by admitting that it "would be very difficult to implement" the method of Bubenik et al. in human patients. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art (emphasis added). See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Since it is clearly evident that even applicant appreciates that multiple administrations of IL-2 would be "very difficult to implement" in human patients, it is clear that expressing IL-2 in an expression vector to avoid multiple administrations would have been knowledge generally available to one of ordinary skill in the art (emphasis added).

In order to establish obviousness, only one motivation is required. However, there is yet another motivation for expressing the IL-2 of Bubenik et al. in the MVA expression vector of Meyer et al. One of ordinary skill in the art at the time the invention was made would have been

motivated to incorporate the IL-2 of Bubenik et al. into the MVA vaccinia vector of Meyer et al. expressing prophylactic L1 and L2 proteins of Lowy et al. and Galloway, and the therapeutic E6 and E7 proteins of Borysiewicz et al. and Galloway, to augment the immune response to the papillomavirus polypeptides, see page 478, Figure 1 on page 479 and the discussion section of Bubenik et al. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for expressing IL-2 in the MVA vaccinia vector of Meyer et al. because Hagensee et al. and Borysiewicz et al. teach expressing papillomavirus polypeptide genes in a vaccinia vector and Meyer et al. use MVA vaccinia virus that allows multiple insertion sites for heterologous inserts. Therefore, one of ordinary skill would have been able to express various papillomavirus polypeptides as well as IL-2 in an MVA vector with a reasonable expectation of success. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Applicant states that the method of Bubenik et al. requires "huge quantities of IL-2" and that expression of IL-2 from a recombinant vector would not enable the quantity of IL-2 required to induce an adjuvanting effect observed by Bubenik et al.

Applicant's arguments have been fully considered, but are found unpersuasive. Regarding the lack of a reasonable expectation of success for expressing the huge quantities of IL-2 administered by Bubenik et al. applicant refers to, the amount of IL-2 administered to laboratory mice to achieve the adjuvanting effect observed by Bubenik et al. would be different from the amount required to achieve the same effect in humans. The amount required to achieve this effect is not a recited element of the claims. Moreover, it is conventional in the vaccine art

to optimize doses, i.e. the amount of MVA vector required to be administered to achieve an efficacious concentration. Differences in concentrations will not support the patentability of subject matter unless there is some evidence indicating that the required concentration is critical to the invention. See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Bubenik et al. clearly establish that IL-2 has immunostimulatory activity and possesses adjuvanting properties against papillomavirus infection. The amount of vector that would be required to be administered to achieve the optimum adjuvanting effect of IL-2 would be a matter of routine experimentation. Applicant's argument that the Office is only speculating that the expression of IL-2 would enable the quantity required for inducing an adjuvanting effect leads the examiner to wonder if applicant is questioning the predictability and quantity of experimentation that would be required to practice the instant invention since applicant also asserts that there is no way to know how to produce the quantities of IL-2 required to influence the immune response in the instant vector composition. It would appear from the teachings in the prior art that this is not the case because the papillomavirus polypeptides required to treat, i.e. E6 and E7, and prevent, i.e. L1 and L2, infection are known. It is also established in the prior art of record that the vaccinia virus vector is an efficient carrier of multiple papillomavirus polypeptide genes and is able to express them simultaneously and in any orientation (i.e. not fused) to induce an effective immune response. It is also established in the prior art that IL-2 induces an effective adjuvant response in a host with compositions against papillomavirus. The ability to express IL-2 from a vaccinia vector is undisputed. The amount of IL-2 required to be expressed from the vector is not claimed and would be a matter of routine optimization in the art. Therefore, a reasonable expectation of success for one of ordinary skill in the art for combining

all of the elements, known in the art to be effective against papillomavirus infection, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lowy et al. (US 5,618,536), Hagensee et al. (Journal of Virology. 1993; 67 (1): 315-322), Borysiewicz et al. (Lancet. June, 1996; 347: 1523-1527), Galloway (Infectious Agents and Disease. 1994; 3: 187-193), Meyer et al. (Journal of General Virology. 1991; 72: 1031-1038), as further evidenced by Boursnell et al. (US 5,719,054), and Bubenik et al. (International Journal of Oncology. 1996; 8: 477-481) as applied to claims 32, 36, 38, 44, 46, 48, 53-56, 62 and 64 above, and further in view of Crook et al. (Cell. 1991; 67: 547-556) and Munger et al. (EMBO Journal. 1989; 8: 4099-4105) for reasons of record.

Applicant reiterates the arguments presented for claim 48, from which claim 49 depends.

These arguments are found unpersuasive and the rejection is maintained for reasons of record. The rebuttal for these arguments is repeated herein.

Claims 65, 69, 71, 72, 74, 79 and 80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borysiewicz et al. (Lancet. June, 1996; 347: 1523-1527), Meyer et al. (Journal of General Virology. 1991; 72: 1031-1038) and Bubenik et al. (International Journal of Oncology. 1996; 8: 477-481), as further evidenced by Boursnell et al. (US 5,719,054) for reasons of record.

Applicant reiterates the summary of the invention. Applicant argues that Boursnell et al. teaches that expressing multiple genes from independent promoters can be difficult to achieve. Applicant also argues that Bubenik et al. fails to provide a reasonable expectation of success

since there would be no way of knowing how to produce huge quantities of IL-2 necessary to influence the immune response since Boursnell et al. teach that expressing more than 2 expression units can be difficult to achieve.

Applicant's arguments have been fully considered, but are found unpersuasive. As pointed out in further teachings of Boursnell et al., difficulties expressing multiple genes from independent promoters is not a hindrance due to new methods briefly mentioned in the reference that eliminate the need for marker genes. Boursnell et al. also expressly illustrate the expression of four different papillomavirus genes from a vaccinia virus vector in Figure 26c.

Regarding the quantity of IL-2 administered to mice by Bubenik et al. to induce an augmenting immune response, Bubenik et al. explicitly teach that IL-2 induces an adjuvanting effect when administered with a composition against papillomavirus. The amount of IL-2 required to be expressed from the instant vector is not a required element. Further, the amount of expression from the instant vector and the amount of vector administered would be of routine design by one of ordinary skill.

Claim 75 is rejected under 35 U.S.C. 103(a) as being unpatentable over Borysiewicz et al. (Lancet. June, 1996; 347: 1523-1527), Meyer et al. (Journal of General Virology. 1991; 72: 1031-1038) and Bubenik et al. (International Journal of Oncology. 1996; 8: 477-481) as applied to claims 65, 69, 71, 72, 74, 79 and 80 above, and further in view of Crook et al. (Cell. 1991; 67: 547-556) and Munger et al. (EMBO Journal. 1989; 8: 4099-4105), as further evidenced by Boursnell et al. (US 5,719,054) for reasons of record.

Applicant reiterates that none of the cited references teach or motivate the skilled artisan to use an MVA vector expressing nonfused papillomavirus polypeptides and an immunostimulatory polypeptide.

These arguments were considered above, but were found unpersuasive. The rebuttal for these arguments is resubmitted herein.

Conclusion

This is a continuation of applicant's earlier Application No. 09/506942. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 10:00 AM - 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley
Primary Examiner
Art Unit 1648